REMARKS

According to the Office Action of August 19, 2009, claims 16, 20, 25, 26, and 31-42 were examined and have been objected to or rejected under 35 U.S.C. § 112, first paragraph, and 35 U.S.C. § 103. In response, Applicants have amended claim 16 and canceled claims 20, 40 and 42. Thus, claims 16, 25, 26, 31-39 and 41 are now pending.

Claim 16 has been amended to incorporate some of the limitations previously presented in claim 20, and claim 20 has consequently been cancelled. Claim 16 was further amended to delete the recitation of "prevention". Thus, no new matter has been added by these amendments.

In view of the amendments to the claims and remarks below, Applicants respectfully request that the rejections be reconsidered and withdrawn.

OBJECTION TO CLAIM 42

The objection asserted against claim 42 is moot as the claim has been cancelled.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ENABLEMENT

Claims 16, 20, 25, 26, 31-39 and 41 have been rejected under 35 U.S.C. § 112, first paragraph. This rejection is moot with regard to claims 20, 40 and 42 because these claims have been cancelled. The Examiner contends that the specification does not reasonably provide enablement for preventing or reducing the risk of the recited diseases or conditions.

Applicants have amended claim 16 to delete the recitation of prevention. Accordingly, this portion of this rejection is now moot.

With regard to "reducing the risk of" limitation, the data presented in the specification establishes a statistically significant increase in delayed type hypersensitivity, reduced Th2 response and Th1/Th2 balancing for animals on a diet comprising the recited oligosaccharides. (See specification at pages 26-28.) The specification further states that "an excessive Th 1 immune response eventually can lead to autoimmunity.... An excessive Th 2

response leads to extreme sensitivity towards foreign components which should not lead to any immunological reaction .... A relative shift towards an increased Th 2 response and/or reduced Th1 response is found under circumstances of stress of any sort, which consequently results in a bias towards a Th 2 response." (Specification at page 1, line 22 to page 2, line 5.)

Thus, the specification provides evidence that the recited method would balance Th1/Th2 levels. Consequently, one of ordinary skill in the art would reasonably expect that by balancing these levels, one would reduce the risk of the recited diseases or conditions because one would understand that an imbalance can lead to autoimmunity or sensitivity.

Precise predictability is not the standard to employ when reviewing enablement. *In re Corpet*, No. 2004-1790, App. No. 09/836,971, 2004 WL 2733634 (BPAI 2004). Instead, the question is whether the invention is reasonably predictable from the information provided.

The above discussed evidence provides one of ordinary skill in the art with sufficient information to conclude that the recited invention reduces the risk of the recited diseases or conditions. In *Corpet*, the examiner recognized that "state of the art recognizes that increased intake of dietary fibers contributes to the increased bowel movements and thus result in lowering the risk of colon cancers." *Id.* at *1. Likewise, in this case, the specification provides that one would recognize that Th1/Th2 levels relate to various autoimmunity and sensitivity conditions. Thus, one would reasonably conclude that balancing those levels would reduce the risk of developing autoimmunity or a sensitivity towards foreign components.

Furthermore, it appears on page 12 of the Office Action that the Examiner acknowledges that treatment of allergies means lowering the risk of allergies, or reduction of risk factors.

For these reasons, the specification provides guidance to make and use the recited invention without undue experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 16, 25, 26, 31-39, and 41 have been rejected under 35 U.S.C. § 112, first paragraph for not being adequately described in the specification. This rejection is moot with regard to claims 20, 40 and 42 because these claims have been cancelled. The Examiner contends that the recitation of "reduction of risk" constitutes new matter because the specification does not use this phrase.[1]

Under 35 U.S.C. § 112, first paragraph, a specification must describe the invention with sufficient detail so that one of ordinary skill in the art would conclude that the inventor had possession of the claimed invention. MPEP § 2163; *Lockwood v. American Airlines, Inc.*, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). Like enablement, the question is whether one of ordinary skill in the art would reasonably understand that the administration of the recited composition, which balances Th1/Th2 levels, would reduce the risk of developing a condition. A verbatim recitation of "reduction of risk" is not necessary.

For the reasons discussed above in the enablement question, one would reasonably understand from the specification that the inventors had in their possession a method of reducing the risk of the recited diseases or conditions because one would understand that balancing Th1/Th2 is an effective means of reducing those risks. Even though the specification does not expressly recite "reduction of risk," the specification, nevertheless, sufficiently describes the invention for this reason. Accordingly, reconsideration and withdrawal are respectfully requested.

REJECTION UNDER 35 U.S.C. § 103

Claims 16, 25, 26, 31-39 and 41 have been rejected under 35 U.S.C. § 103 as being unpatentable over Ikemizu[2] in combination with Okada[3], Nagura[4] and Miniello[5]. This

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[1] Office Action of August 19, 2009 at page 8.
[2] JP 2003-221339 to Ikemizu *et al.* ("Ikemizu").
[3] EP 1 321 527 to Okada *et al.* ("Okada").
[4] Nagura *et al.*, "Suppressive effect of dietary raffinose on T-helper 2 cell-mediated immunity," BRITISH J. OF NUTR. (2002) 88: 421-426 ("Nagura").
[5] Miniello *et al.*, "Prebiotics in infant milk formulas: new perspectives," ACTA PÆDITR. SUPPL. (2003) 441: 68-76 ("Miniello").

rejection is moot with regard to claims 20, 40 and 42 because these claims have been cancelled.

I. RECITED INVENTION

The invention, as recited in amended claim 16, is directed to a method for the treatment or reduction of risk of an immune system-related disorder in a mammal. The immune system-related disorder is selected from the group consisting of allergy Type 1, allergy Type 2, allergy Type 3, and allergy Type 4. The method comprises administering to the mammal a composition comprising a therapeutically effective amount of an acid oligosaccharide and two chemically distinct neutral oligosaccharides. The acid oligosaccharide has a degree of polymerization between 1 and 250 and is prepared from pectin or alginate. The acid oligosaccharide comprises at least one terminal uronic acid unit selected from the group consisting of galacturonic acid, guluronic acid and mannuronic acid. The two chemically distinct neutral oligosaccharides comprising fructooligosaccharides and a second oligosaccharide selected from the group consisting of transgalactooligosaccharides, galactooligosaccharides and mixtures thereof.

II. DIFFERENCES BETWEEN THE CITED REFERENCES AND THE CLAIMED INVENTION

Ikemizu discloses acid xylooligosaccharide,[6] which is not the recited acid oligosaccharide – they do not have at least one terminal uronic acid unit selected from the group consisting of galacturonic acid, guluronic acid and mannuronic acid as recited in claim 16. Ikemizu's xylooligosaccharide has a xylose backbone where an uronic acid residue is attached as a side chain.[7] Xylooligosaccharides are made from xylose units. The uronic acid side chains disclosed in Ikemizu are glucuronic acid or 4-O-methyl-glucuronic acid; and therefore derived from glucose, not galactose, mannose or gulose.[8]

In contrast, the recited invention requires that the acid oligosaccharide be prepared from pectin or alginate. Pectin is a linear chain of α-(1-4)-linked D-galacturonic acid units. Within this backbone, D-galacturonic acid units are occasionally replaced with L-

[6] Ikemizu at abstract.
[7] Ikemizu at translated page 3.
[8] Ikemizu at translated page 3.

rhamnose units. Neutral sugars, such as xylose, may branch from these L-rhamnose units. Thus, while pectin may contain xylose, it is not a xylooligosaccharide as disclosed in Ikemizu.

Likewise, alginates are not xylooligosaccharides. Alginates are linear unbranched polymers containing β-(1-4)-linked D-mannuronic acid and α-(1-4)-linked guluronic acid residues.[9] It does not contain xylose; and therefore, it is not a xylooligosaccharide.

Neither pectin nor alginate would produce a xylooligosaccharide, nor would they have an uronic acid side chain. Only pectin comprises xylose, but xylose is not the backbone. Instead, it is a sugar residue that branches from the D-galacturonic acid backbone. Consequently, an acid oligosaccharide prepared from pectin or alginate could not have a xylose backbone with uronic acid side chains. Thus, in addition to the fact that Ikemizu does not teach administering a compound to treat immune system-related disorders, or the use of neutral oligosaccharides, it additionally does not teach the recited acid oligosaccharide.

Additionally, uronic acid units themselves are different. Ikemizu discloses that the uronic acids residues are glucuronic acid or 4-O-methyl-glucuronic acids. Therefore, the acid residues are derived from glucose. In contrast, alginate contains mannuronic acid and guluronic acid residues; and pectin contains galacturonic acid units. Therefore, the uronic acid units in pectin and alginate are derived from galactose, mannose and guluose. Consequently, these uronic acid units disclosed in Ikemizu are different from those in pectin or alginate.

According to the Office Action, Okada, teaches that atopic dermatitis can be treated with raffinose, an α-galactosyl oligosaccharide or netrual oligosaccharide. However, Okada does not teach or suggest that xylooligosaccharides or acid oligosaccharide prepared from pectin or alginate can be used instead of an α-galactosyl oligosaccharide. Nor does Okada teach or suggest using two chemically distinct neutral oligosaccharides comprising

[9] Specification at page 13, lines 11-12.

fructooligosaccharides and a second oligosaccharide selected from the group consisting of transgalactooligosaccharides, galactooligosaccharides and mixtures thereof.

III. ARGUMENT

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a *prima facie* case of obviousness. *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). To establish this, each and every claimed element must be taught or made obvious by the applied references. *Ex parte Hellums*, App. No. 09/103,704, 2003 WL 25281923 at *4 (BPAI Jul. 15, 2003); *Ex parte Likins*, App. No. 10/010,392, Appeal No. 2004-0760, 2004 WL 4981756 at *3 (BPAI Apr. 8, 2004).

As discussed above, the references do not teach an acid oligosaccharide prepared from pectin or alginate that comprises at least one terminal uronic acid unit selected from the group consisting of galacturonic acid, guluronic acid and mannuronic acid. Furthermore, the references do not teach using two chemically distinct neutral oligosaccharides comprising fructooligosaccharides and a second oligosaccharide selected from the group consisting of transgalactooligosaccharides, galactooligosaccharides and mixtures thereof.

The Patent Office must further establish some reason to combine the references. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1731 (2007); *Takeda Chemical Industries, Ltd. v. Alpharpharm Pty., Ltd.*, 492 F.3d 1350, 1356-1357 (Fed. Cir. 2007). The *KSR Int'l* Court acknowledged the importance of identifying a reason that would have prompted a person of ordinary skill in the art to combine the elements in the way the claimed invention does. *KSR Int'l*, 127 S.Ct. at 1731; *Takeda Chemical*, 492 F.3d at 1356-1357. Repeatedly throughout the *KSR Int'l* decision, the Court discussed the importance that the result obtained by a particular combination was predictable to one of ordinary skill in the art. *KSR Int'l*, 127 S.Ct. at 1731 and 1739-1742.

Here, there is no reason to substitute Ikemizu's xylooligosaccharides with the recited acid oligosaccharides that comprise at least one terminal uronic acid unit selected from the group consisting of galacturonic acid, guluronic acid and mannuronic acid. One of

ordinary skill in the art would not reasonably believe that oligosaccharides having different structures are equivalent or can be substituted for one another. Instead, one would expect different oligosaccharides to have completely different effects. Therefore, one would not have a reason to replace one oligosaccharide, such as Ikemizu's xylooligosaccharide, with another, such as the recited acid oligosaccharides prepared from pectin or alginate and having at least one terminal uronic acid unit selected from the group consisting of galacturonic acid, guluronic acid and mannuronic acid, because one would not reasonably expect the effects to be the same. Furthermore, there is no reason to substitute Okada's neutral oligosaccharides with those recited in claim 16.

In addition to the above reasons, the specification provides data of an unexpected synergistic effect when the recited invention is practiced. For example, Table 3 (specification at page 27) shows that the combination of AcOl and GF synergistically lowers the antigen specific proliferation. For the Examiner's convenience, Table 3 is reproduced below.

TABLE 3

Wt. % oligosaccharides in diet	Influvac specific proliferation (%)
0 (control)	100
1 wt % GF	100
1 wt. % AcOl	92
2.5 wt. % AcOl	61*
5 wt. % AcOl	54*
1 wt. % GF and 1 wt. % AcOl	50*

*indicates significantly different ($P < 0.05$) from control

Thus, the specification provides evidence that an acid oligosaccharide and two chemically distinct neutral oligosaccharides act synergistically, which was not expected. For example, GF alone had no effect on antigien specific proliferation; however, when co-administered with AcOL, it lowered the antigen specific proliferation from 92% to 50%.

Assuming that a *prima facie* case of obviousness has been established (which the Applicants expressly deny), these unexpected results rebut the obviousness rejection. *Ormco Corp. v. Align Technology, Inc.*, 463 F.3d 1299, 1311, 79 U.S.P.Q.2d 1931 (Fed. Cir. 2006); MPEP § 2145; *see also In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995). To establish unexpected results, the Applicant must

> establish (1) that there actually is a difference between the results obtained through the claimed invention and those of the prior art, *In re Klosak*, 455 F.2d 1077, 59 CCPA 862 (1972); and (2) that the difference actually obtained would not have been expected by one skilled in the art at the time of invention, *Id.*; *In re D'Ancicco*, 439 F.2d 1244, 58 CCPA 1057 (1971).

In re Freeman, 474 F.2d 1318, 1324 (CCPA 1973). Without evidence to the contrary, an applicant need only provide substantially improved results and state that the results were unexpected. *Soni*, 54 F.3d at 750; *In re Lee*, App No. 10/091,061, 2007 WL 176690 at *3 (BPAI June 19, 2007).

In *Soni*, the examiner rejected certain claims as obvious in view of a combination of references. The applicant directed the examiner to the data in the specification, and argued that the increase in tensile strength and the increase in peel strength rebutted the rejections. *Soni*, 54 F.3d at 747. On appeal to the Federal Circuit, it was argued that the Board

> could have taken judicial notice of the fact that higher molecular weight polymers would have been expected to tolerate higher filler loadings without degradation in properties and that it could have taken notice of the fact that it is the polymer *per se* that primarily determines the mechanical properties of a filled polymer composition.

Id. at 750. However, the Federal Circuit found this argument fatally flawed because the Board failed to support its position with facts or evidence. *Id.* at 750; *see also Lee*, 2007 WL 176690 at *3. In summary, the Federal Circuit held that

> [m]ere improvement in properties does not always suffice to show unexpected results. In our view, however, when an applicant demonstrates *substantially* improved results, as Soni did here, and *states* that the results were *unexpected,* this should suffice to establish unexpected results *in the absence of* evidence to the contrary.

Soni, 54 F.3d at 751.

Here, the Applicants have provided evidence of an actual difference, and this difference was unexpected. Accordingly, assuming that a *prima facie* case of obviousness has been established, these unexpected results rebut the *prima facie* case.

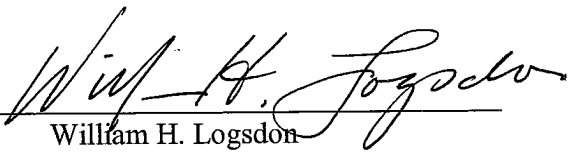
CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that all pending claims 16, 25, 26, 31-39 and 41 in the instant application are patentable over the cited references and are in condition for allowance. Accordingly, reconsideration and withdrawal of the asserted rejections and a Notice of Allowance are respectfully requested.

Should the Examiner have any questions or concerns, the Examiner is invited to contact the Applicants' undersigned attorney by telephone at 412-471-8815.

Respectfully submitted,

THE WEBB LAW FIRM

By 

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